Remarks / Arguments

Claims 1-6 and 10-12 are pending in this application. Claim 1 has been amended to further characterize pluripotential cells in that they have the potential of expressing either macrophage or dendritic cell characteristics. Support for this amendment can be found throughout the specification, for example, at page 6, lines 10-12. No new matter has been added by way of these amendments.

The Office Action has acknowledged that the Application is a continuation of parent application (Serial No. 08/600,483).

After entry of the amendment, claims 1-6 and 10-12 will be pending in the Application. Applicants respectfully request reconsideration of pending claims 1-6 and 10-12 in view of the amendment to the claims and the following remarks.

I. The Claims Meet the Requirements of 35 U.S.C. § 112, Second Paragraph.

Claims 1-6 and 10-12 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for recitation of "pluripotential cells."

Applicants respectfully traverse this ground of rejection.

As an initial matter, in their Amendment filed October 2, 2003, Applicant did not allege that the term, "pluripotential cells," was defined in the specification at page 14, lines 16-24 or page 22, lines 18-19. Rather, the Applicants in their previous Amendment referenced the specification at page 14, lines 16-24 or page 22, lines 18-19 to describe the reversion of immature dendritic cells back to pluripotential cells if they are not exposed to a factor.[1]

As discussed in their Amendment filed October 2, 2003, Applicants posit that based on the standard dictionary definition of the term "pluripotent," the ordinarily skilled artisan would understand the metes and bounds of the claimed invention.

[1] Full quote from page 5 of the Amendment filed October 2, 2003 is: "Applicants note that the specification teaches that although immature dendritic cells can be produced by pluripotent cells, unless immature dendritic cells are exposed to a factor (*e.g.*, a dendritic cell maturation factor), they will revert back to being pluripotential cells having characteristics similar to macrophages or monocytes (see, *e.g.*, specification at page 14, lines 16-24 and at page 22, lines 18-19)."

However, in order to facilitate prosecution, Applicants have further clarified that the pluripotential cells of the claim are those cells "having the potential of expressing either macrophage or dendritic cell characteristics." Thus, Applicants respectfully aver that the claims have now met the requirements of 35 U.S.C. §112, second paragraph, and, as such, this rejection should be reconsidered and withdrawn.

II. The Claims Meet the Requirements of 35 U.S.C. § 102.

Claims 1-6 and 10-12 stand rejected under 35 U.S.C. §102(e) as being allegedly anticipated by U.S.P.N. 5,994,126 ("the '126 patent") and under 35 U.S.C. §102(b) as being allegedly anticipated by Romani *et al.*, *J. Exp. Med.* 180: 83-93, 1994 ("Romani").

Applicants respectfully traverse these grounds for rejection.

Applicants have addressed these rejections together because the Application differs fundamentally from both of these references--while both of these references describe methods to generate *immature* dendritic cells, the present Application teaches methods for generating ***mature*** dendritic cells from either immature dendritic cells or pluripotential cells. Applicants, in their Amendment filed October 2, 2003, specified that mature dendritic cells have the following characteristics: increased CD83 expression, increased CD86 expression, decreased CD115 expression, or decreased CD32 expression relative to pluripotential cells. This amendment to the claims was made to further clarify the differences between mature dendritic cells and immature dendritic cells or pluripotential cells.

The methods described by the '126 patent and by Romani merely result in the production of immature dendritic cells, that is, a cell that, once removed from the cytokines used to produce it, reverts back to a pluripotential cell having characteristics similar to macrophages (see specification at page 14, lines 16-24). Indeed, the Application teaches, at page 16, lines 25-27, that the method of Romani can be used to generate *immature* dendritic cells. It is the further maturation of these immature dendritic cells into stable mature dendritic cells that is one of the major features of the present invention. While it was known prior to the Application that "dendritic cells" could be generated by culturing adherent blood fractions in different cytokines (*e.g.*, Romani describes culturing cord blood or adult blood in GM-CSF plus TNF-α or GM-CSF

plus IL-4), the Application describes the discovery that these so-called "dendritic cells" were, in fact, unstable, and reverted to pluripotential cells upon withdrawal of the cytokines. It is only upon the culture of immature dendritic cells or pluripotential cells in the presence of a factor (*e.g.*, a dendritic cell maturation factor), that stable mature dendritic cells are obtained.

Accordingly, Applicants' characterization of the mature dendritic cells produced by the methods of the claimed invention in having increased CD83 expression, increased CD86 expression, decreased CD115 expression, or decreased CD32 expression relative to pluripotential cells is **not** merely a further characterization of the cells produced by the methods described by the '126 patent and Romani. Indeed, each of Romani and the '126 patent fails to discuss changes in any of CD83, CD86, or CD115 because these cell surface markers are not important in distinguishing the "dendritic cells" their methods produced. Further, although Romani does discuss CD32 (note that the '126 patent does not), as shown in Fig. 5 (left column) of that reference, the "dendritic cells" of Romani show high expression of CD32, while on the distinguishing features of the mature dendritic cells of the invention is that the expression of CD32 is *decreased.*

Thus, Applicants aver that their invention, as presently claimed, is novel and unanticipated by either of Romani or the '126 patent. Based on these remarks, Applicants respectfully aver that the claims meet the requirements of 35 U.S.C. §102, and therefore respectfully request this rejection should be reconsidered and withdrawn.

III. The Claims Meet the Requirements of 35 U.S.C. § 112, First Paragraph.

Claims 1-6 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, because "there is insufficient written description to how that Applicant was in possession of a factor in which to culture pluripotential cells which would case them to express characteristics of DCs..." (Office Action, p. 4).

Applicants respectfully traverse this ground of rejection.

As Applicants have previously asserted in their Amendment filed October 2, 2003, those of ordinary skill in the art, upon reading the specification, would realize that if they cultured pluripotential cells in the presence of a factor (*e.g.*, a dendritic cell maturation factor), they

would obtain mature dendritic cells, and would realize that they would not obtain mature dendritic cells if the pluripotential cells were cultured in the absence of the factor. Indeed, Applicants' specification has provided two sources for the factor, namely conditioned medium and fixed *Staphyloccus aureus* (SACS) (see, *e.g.*, page 47, line 14 through page 54, line 25). Thus, Applicants respectfully aver that the ordinarily skilled artisan would conclude, upon reading the specification, that Applicants possessed the claimed invention at the time the Application was filed.

The Office Action has asserted that to overcome this ground for rejection, the Applicants must identify the factor, and that simply supplying a source for the factor will not overcome this ground for rejection (Office Action, p. 5).

Applicants respectfully point out that current caselaw does not support the position taken by the Office Action.

The Federal Circuit has recently held that "reference in the specification to a deposit made in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement." Enzo Biochem v. Gen-Probe Inc., 323 F.3d 956, 965 (Fed. Cir. 2002). In Enzo, the claims were product by process claims, where the process employed purified chromosomal DNA from different bacterial strains which had been deposited with the American Type Culture Collection. Id. at 961. The Federal Circuit stated that "Although the structures of those sequences, *i.e.*, the exact nucleotide base pairs, are not expressly set forth in the specification, those structures may not have been reasonably obtainable and in any event were not known to Enzo when it filed its application 1986...We therefore agree with Enzo that reference in the specification to deposits of nucleotide sequences describe those sequences sufficiently to the public for purposes of meeting the written description requirement." Id. at 966.

Applicants respectfully aver that the parallel between the patent at issue in Enzo and the Application is determinative. Like Enzo, the Application describes the source for a factor (*e.g.*, a dendritic cell maturation factor); however, the exact factor was not reasonably obtainable at the time the application was filed. (see Id.). Thus, for the same reasons that the patent of Enzo was

held as meeting the written description requirements of 35 U.S.C. § 112, first paragraph, so too should the present Application.

Applicants also note that in a recent case where a patent was held invalid for lack of written description support, the patent claimed a method using a compound but disclosed neither the compound nor any suggestions as to how the compound could be made or otherwise obtained. Univ. of Rochester v. G.D. Searle & Co., 357 F.3d 916, 919 (Fed. Cir. 2004). In contrast to the patent at issue in Univ. of Rochester, the present Application provides two sources for the factor used in the claimed method (see Id.). Moreover, according to the Federal Circuit, the claimed methods in the Univ. of Rochester case "cannot be practice based on the patent's specification, even considering the knowledge of one skilled in the art." Univ. of Rochester at 927. In the present Application, given the two different sources of the factor described in the specification, the ordinarily skilled artisan could easily practice the claimed method.

Thus, for the foregoing reasons, claims 1-6 and 10-12 meet the requirements of 35 U.S.C. § 112, first paragraph (written description).

Claims 1-6 and 10-12 also stand rejected under 35 U.S.C. § 112, first paragraph, because the claim language added in their Amendment filed Oct. 2, 2003, namely "decreased CD115 expression, and decreased CD32 expression relative to the pluripotential cells," is allegedly new matter because page 27 of the specification discloses only "loss of CD115 and CD32 expression and no comparison to pluripotential cells" (Office Action, page 5, emphasis in original).

Applicants respectfully traverse this ground for rejection.

First of all, in their Amendment filed Oct. 2, 2003, Applicants pointed to page 17 as an example of a region in the specification supporting the added claim language. Additional support can also be found in the specification at, for example, page 55, line 16 through page 56, line 9. There, at page 55, line 27-30, the specification describes the down-regulation of CD32. The ordinarily skilled artisan would understand that down-regulation does not mean total loss. Additionally, in Fig. 7, the results of which are summarized, in part, at page 55, line 16 through page 56, line 9 of the specification, the CD115 marker is clearly reduced, yet not lost (i.e.,

absent) as compared to starting immature dendritic cells (compare B to B'). In other words, the expression of CD115 is *decreased* on the mature dendritic cells.

Finally, with respect to the language "relative to the pluripotential cells," Applicants aver that it is clear from the specification that these markers are reduced relative to the starting pluripotential cells. For example, in Fig. 7, all of the markers shown are compared to starting immature dendritic cells. More relevantly, when the specification described a marker (*e.g.*, CD32) as being down-regulated on a mature dendritic cell, it is implicit that the mature dendritic cell is being compared to the starting pluripotential cell. According to the Federal Circuit, the specification satisfies the description requirement even if the claimed subject matter is not described *in haec verba* in the specification, as long ordinarily skilled artisan, upon reading the specification, is able to immediately discern the limitation at issue in the claims. Purdue Pharma L.P. v. Faulding Services, Inc., 230 F.3d 132, 1323 (Fed. Cir. 2000). Here, it is clear that the stated characteristics of dendritic cells produced by the claimed method are being compared to those characteristics on the starting pluripotential cell.

Accordingly, Applicants aver that claims 1-6 and 10-12 meet the requirements of 35 U.S.C. § 112, first paragraph, as far as this new matter rejection is concerned.

Based on the foregoing remarks, these 35 U.S.C. § 112, first paragraph, rejections should be reconsidered and withdrawn.

Conclusion

Applicant posits that the presently maintained rejections of the pending claims have been fully overcome by amendment and/or argument. Accordingly, Applicant respectfully submits that the pending claims are in condition for allowance. If the Examiner believes that any further discussion of this communication would be helpful, he is encouraged to contact the undersigned by telephone.

In addition to the fee required for the accompanying Request for Continued Examination, no fees are believed to be due in connection with this communication. However, please apply any additional charges, or credit any overpayment, to our Deposit Account No. 08-0219.

Respectfully submitted,
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Date: April 16, 2004

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